

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
)
Dietrich BRANDENBURG et al.) Group Art Unit: Unassigned
)
Serial No.: Unassigned) Examiner: Unassigned
)
Filed: Concurrently herewith)
)
For: COVALENTLY BRIDGED INSULIN)
DIMERS)
)

being a **Continuation** of International Application No. PCT/EP00/01530 filed February 24, 2000.

BOX PATENT APPLICATION
Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Before examining this application, please amend the application as follows:

IN THE SPECIFICATION:

Please amend the specification as follows:

Page 1, after the title, insert a new paragraph as follows:

-- CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation of International Application No.

PCT/EP00/01530, filed February 24, 2000, which is incorporated by reference herein

and claims the priority of DE 199 08 041.0 filed February 24, 1999, which is

incorporated by reference herein.--

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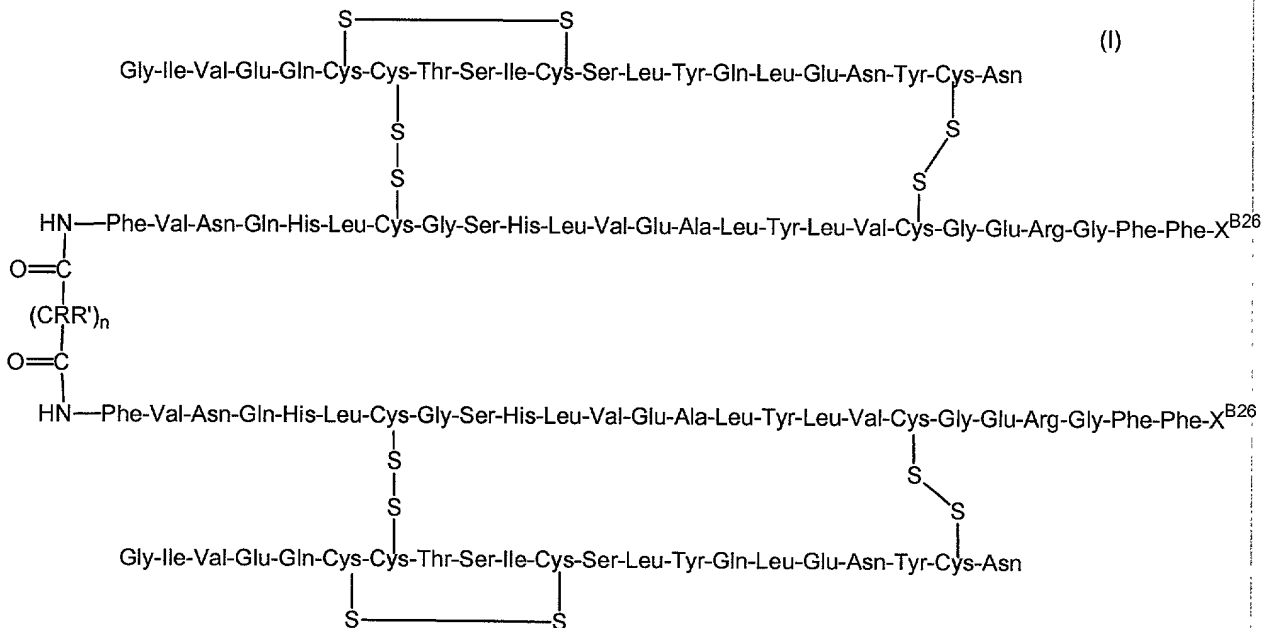
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IN THE CLAIMS:

Please cancel claims 1-14 without prejudice or disclaimer and substitute new claims 15-36 therefor as follows:

15. An insulin analogue consisting of two identical or different insulin monomers covalently linked together via a bridge,
wherein the insulin monomers are selected from a group comprising human insulin, animal insulins and derivatives of human insulin and animal insulins,
wherein at least one derivative of human insulin or of an animal insulin is present in an insulin analogue,
and physiologically acceptable salts thereof.

16. The insulin analogue as claimed in claim 15, characterized by formula I,



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wherein:

- a) X is, independently of one another, a branched or unbranched C₁-C₁₀-alkyl group, a mono- or polysubstituted aryl group, a C₁-C₁₀-alkyl group, mono- or polysubstituted or unsubstituted O-aryl group, an amino acid or a derivative thereof, or a group of the formula nRR', wherein
- b) each of R and R' is H, NH₂, a branched or unbranched C₁-C₁₀-alkyl radical, or a mono- or polysubstituted or unsubstituted aryl group, and wherein
- c) n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16.

17. The insulin analogue as claimed in claim 16, wherein X is an amino acid in which the carboxylic acid group is amidated.

18. The insulin analogue as claimed in claim 17, wherein X is the amino acid sarcosine.

19. The insulin analogue as claimed in claim 16, wherein the X residues in the two B chains are different from one another.

20. The insulin analogue as claimed in claim 16, wherein X is an amino group.

21. B1,B1'-Sub-[Sar^{B26}]-des-(B27-B30)-insulin-B26-amide insulin dimer.

22. B1,B1'-Sub-[D-Ala^{B26}]-des-(B27-B30)-insulin-B26-amide insulin dimer.

23. B1,B1'-Sub-[Glu^{B26}]-des-(B27-B30)-insulin-B26-amide insulin dimer.

24. A pharmaceutical preparation, comprising

- a) an insulin analogue as claimed in claim 15, and

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- b) additions selected from the group comprising zinc salts, phenol, m-cresol, glycerol, and buffer substances.
25. A pharmaceutical preparation, comprising
- a) an insulin analogue as claimed in claim 21, and
- b) additions selected from the group comprising zinc salts, phenol, m-cresol, glycerol, and buffer substances.
26. A pharmaceutical preparation, comprising
- a) an insulin analogue as claimed in claim 22, and
- b) additions selected from the group comprising zinc salts, phenol, m-cresol, glycerol, and buffer substances.
27. A pharmaceutical preparation, comprising
- a) an insulin analogue as claimed in claim 23, and
- b) additions selected from the group comprising zinc salts, phenol, m-cresol, glycerol, and buffer substances.
28. A method for treating diabetes, comprising administering the pharmaceutical as claimed in claim 24 to a host that has diabetes.
29. A method for treating diabetes, comprising administering the pharmaceutical as claimed in claim 25 to a host that has diabetes.
30. A method for treating diabetes, comprising administering the pharmaceutical as claimed in claim 26 to a host that has diabetes.
31. A method for treating diabetes, comprising administering the pharmaceutical as claimed in claim 27 to a host that has diabetes.

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32. A diagnostic kit comprising one or more of the insulin analogues as claimed in claim 15.
33. A diagnostic kit comprising one or more of the insulin analogues as claimed in claim 21.
34. A diagnostic kit comprising one or more of the insulin analogues as claimed in claim 22.
35. A diagnostic kit comprising one or more of the insulin analogues as claimed in claim 23.
36. A method for preparing an insulin analogue as claimed in claim 15, wherein
- (a) the monomeric insulin analogues are obtained by enzyme-catalyzed semisynthesis or by methods of genetic manipulation,
 - (b) the monomeric insulin analogues from step (a) are optionally partially protected by protective groups;
 - (c) the protected monomeric insulin analogues from step (b) and/or the monomeric insulin analogues from step (a) are reacted with a preactivated dicarboxylic acid, and
 - (d) the insulin analogues obtained in step (c) are isolated from the reaction mixture.

REMARKS

New claims have been substituted for the original claims to conform them to U.S. practice and to eliminate improper multiple dependency. Claims 15-36 are pending in this application. No new matter has been added.

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